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PAIN MANAGEMENT IN NEUROLOGY

ARTICLE 1: PRINCIPLES OF PAIN MANAGEMENT

Beth B. Hogans, MS (Biomath), MD, PhD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1318–1343.

ABSTRACT

OBJECTIVE:

This article introduces the general principles of assessing, diagnosing, and managing pain relevant to neurologic practice.

LATEST DEVELOPMENTS:

Scientific understanding of and clinical practices related to pain and pain management are advancing. The field is remarkable for the diversity of health professions engaged in this effort, including physicians, scientists, psychologists, pharmacists, and many others. Pain classification is transforming with pending changes to the *International Classification of Diseases* diagnostic coding system, and pain assessment has moved toward consistent application of the biopsychosocial model. The diagnosis of pain has continued to become more sophisticated with the development of additional testing modalities, clearer classification systems, and diagnostic criteria. Pain management requires both pharmacologic and nonpharmacologic elements; systematic review evidence for both of these and interventional and surgical management are increasingly available. The context of treatment remains important given the impact of social determinants of health and limitations of access to diagnostic and treatment resources. Due to global and interprofessional collaborations as well as new research funding, the outlook is positive.

ESSENTIAL POINTS:

Pain is a protean experience for humans; functional MRI (fMRI) and other research modalities show that pain perception is highly multifocal, and modulation occurs at many nervous system levels. Neurologists bring special skills to pain evaluation and management, are well equipped to appreciate both the focal and diffuse nature of pain, and can envision how pain attenuates sleep, cognitive function, mobility, motivation, and social connection. By operationalizing expert knowledge of the nervous system, implementing relevant therapies, and collaborating with diverse health professions to manage pain, neurologists can succeed at and find meaning in optimizing patient outcomes.

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KEY POINTS

- The systematic classification of facial pain and headache disorders in the International Classification of Headache Disorders allows for relatively detailed diagnoses of these disorders in both inpatient and outpatient neurology settings that are consistent from one location to another.
- The neurologic management of headache and facial pain includes acknowledging the patient's experience of pain and related symptoms; seeking diagnostic information through neurologic examination and diagnostic testing; and integrative management including pharmacologic and nonpharmacologic therapies, potentially incorporating lifestyle modifications using a "whole-health" approach and interprofessional collaboration.
- Pathologic processes giving rise to spine pain can be biomechanical, musculoskeletal, neuropathic, nociplastic, central sensitization mediated, infectious, and immune mediated.
- Common neuropathic pain patterns include a distal symmetrical gradient-type pattern, neuropathy affecting only small fibers (typically diffusely distributed), "named nerve" patterns, radicular (dermatomal) patterns, and visceral involvement patterns.
- There are no well-established clinical tests currently used to determine the presence of central sensitization.
- Given the frequency with which patients with complex pain conditions are encountered in clinical practice, neurologists need to know that several pain mechanisms may be active at any phase of treatment.
- It is often necessary to initiate symptomatic pain treatment concurrently with the diagnostic workup so that patients do not continue to experience uncontrolled pain while awaiting test results.
- New pain classification systems will require a major revision to coding practices as practitioners will be expected to distinguish both pain mechanisms and underlying pathologies.
- Features of pain presentation of particular interest include symptom quality, region, severity, and timing, as well as identifying factors that alleviate and worsen the symptoms.
- In the diagnosis of pain-associated conditions, there is a role for the assessment of musculoskeletal dysfunction.
- Pain may impact motor, cerebellar, and cognitive function, but these effects will vary by etiology.
- Health systems vary in terms of both the opportunities for interprofessional collaborative care for patients with chronic pain and the provision of a broad range of therapies.
- Interprofessional collaboration and the principles of teamwork, communication, ethics and values, and the responsibility and roles of other professions can deliver pain care that is patient-centered and responsive to the community's needs.
- Normal nociceptive processing, like all somatosensory signals, involves (1) transduction, the process of translating external energy (eg, heat, cold, pressure) into action potentials; (2) transmission, which carries information from the peripheral sensing structures to the spinal and supraspinal centers; (3) modulation, which tempers the flow of information; and (4) perception, which for pain is highly multicentric.
- The development of an appropriate differential diagnosis requires knowledge of the most relevant common pain-associated conditions as well as those that are potentially catastrophic.
- For structural spine lesions, imaging is typically considered the definitive diagnostic test, although, in the context of suspected nerve or root compression, nerve conduction studies and EMG may be necessary to appraise functional impact.
- For many patients, a helpful approach is to invite the patient to identify the psychosocial factors that they believe are important to their current pain management.
- Neurologists should be vigilant and diligent in screening for affective disorders and suicidality as the risk for suicide is increased for patients with chronic pain.
- Even modest amounts of pain may worsen sleep quality and limit sleep duration; at the same time, poor quality and limited duration of sleep will limit patients' self-modulatory pain mechanisms.
- Motivational interviewing and acceptance and commitment therapy, which focuses on pursuing activities that have the greatest personal meaning, can be very helpful for prioritizing activities and selecting therapies for patients who have pain.

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- Disability related to pain can be the most important aspect of a patient's experience of pain. For some patients, pain entails motor impairment, dyscoordination, or autonomic dysregulation.
- Pharmacologic and nonpharmacologic management are both important to optimize pain control while minimizing problematic side effects.
- All pain-active antidepressants carry a boxed warning for suicidality risks; these should be explained to patients and instructions for how to respond in the event of suicidal ideation should be provided.
- Nonpharmacologic therapies for pain-associated conditions managed in neurology practice continue to accrue evidence of measurable benefits.
- Physical activity is important for many reasons, including the upregulation of endogenous analgesic mechanisms and preservation of function, and psychological support is important to reduce pain-related interference with function, suffering, and pain intensity.
- Incorporating coordinated nonpharmacologic therapies can reduce pharmacologic focus and polypharmacy, which is associated with cognitive interference and increased falls in older adults and accidental injury, substance use disorders, and long-term dependency in passive pain relief strategies.
- By working with collaborating providers (eg, physical therapists and clinical psychologists), patients will make important and helpful connections that foster a proactive dynamic toward pain, including increased pain self-efficacy.
- Neurologists bring a special skill set to pain management, with advanced training in neurologic localization, familiarity with issues pertaining to impairment and disability, and expert knowledge of several medications used for chronic pain.

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ARTICLE 2: SPINE PAIN

Vernon B. Williams, MD, FAAN. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1344–1362.

ABSTRACT

OBJECTIVE:

Spine pain is one of the most common presenting concerns in health care settings. This article reviews clinical strategies for evaluating and managing patients with spine pain.

LATEST DEVELOPMENTS:

Minimally invasive interventional procedures, virtual reality, predictive analytics, neuromodulation, and other evolving technologies are significantly impacting the management of spine pain. Advances in modern pain science have also led to effective skills and treatment strategies, including patient interviews and queries for insight regarding pain, education, and cognitive restructuring, and adjusting the timing of examination (after reeducation) and examination techniques to encourage the experience of movement in the absence of assumed tissue damage. An evolving understanding of the influence of patient-centric thoughts, framing, emotional status, and cognitive restructuring's influence on the brain's response to perceived threat are important aspects of spine pain management.

ESSENTIAL POINTS:

The correlation of clinical presentations with structural abnormalities is necessary but insufficient to evaluate and manage spine pain. Modern pain science acknowledges pain as a subjective experience but recognizes a critical distinction between tissue damage, nociception, and the experience of pain. What and how we communicate with patients, as well as evolving neuromodulation technologies, augment conventional approaches.

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KEY POINTS

- Many patients with spine pain conceive of and frame their experience as the direct and sole result of physical stimuli ("pain signals") resulting from tissue damage. Modern pain science recognizes the inadequacy of this simplistic concept.
- Modern pain science establishes additional factors such as expectation, the brain's processing and interpretation of sensory input, variations in nociceptive thresholds, and other factors that are critical to the pain experience.
- Modern pain science and emerging theories related to the experience of pain involve far more complex physiologic activity than the ascending and descending pain nervous system pathways typically used to show nociceptive and modulating signals.
- Pain is defined as an unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage.
- Communication with patients who have spine pain should reinforce concepts related to modern pain science. Without vigilant attention, actions and words can negatively impact patient insight, framing, and outcome.
- When devising spine pain management strategies, the consideration of neuroplasticity will involve an expanded appreciation of biological factors (at the level of the spinal cord, within the brain, and distributed throughout the body) contributing to the pain experience and prevent inappropriate and sole focus on the simple treatment of a peripheral anatomic spine "pain generator."
- Likely owing to the maladaptive effects of neuroplasticity with time, chronic pain becomes less specific relative to location.
- Axial pain without significant radiation into the legs (particularly below the knee) suggests vertebral body, diskogenic, facet, sacroiliac, or muscular conditions.
- Radicular or radiating pain from the spine into one arm or leg suggests nerve root compression, whereas pain radiating from the spine into both arms or both legs symmetrically suggests an intraspinal condition.
- Provocative testing is a crucial aspect of the clinical evaluation of spine pain.
- Routine imaging for individuals with spine pain who have nonspecific symptoms, no red flags, and have not had appropriate trials of conservative treatments can be costly, ineffective, and may contribute negatively to patient outcomes.
- Cultural beliefs, past experiences, personal values, family or financial concerns, or other priorities may reasonably influence management decisions for patients with spine pain.
- Alternative routes of administration and nontraditional forms of analgesics should be considered to minimize risk, minimize side effects, maximize safety profile, and optimize effect in patients with spine pain.
- Drug formulations with rapid onset of action, long-acting or gradual absorption, or those that do not require traditional gastrointestinal absorption (eg, intranasal, transmucosal, and transdermal versions of anti-inflammatories, partial agonist opioids) may be safer and more effective alternatives to consider in appropriate candidates with spine pain.
- Diagnostic injections for spine pain should be limited to local anesthetic and not include steroids, which can confound the interpretation of results.
- Pain diaries or other strategies that allow for the review of the patient's response as documented in real time may be more accurate than retrospective description, memory, or the misinterpretation of a temporary effect as ineffective.
- Increasingly, and in concert with increasing experience and insight regarding neuroplasticity, neuromodulation strategies are being successfully employed in the treatment of spine pain. Moreover, the use of these strategies is no longer limited to a "last resort" or in the event of inadequate response to other intervention trials.
- Surgical intervention in the spine can be categorized relative to the goal of decompression, fusion to reduce maladaptive motion, or disk replacement to facilitate motion.
- Health equity, health disparities, and social determinants of health must be recognized in light of the

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inevitable and inarguable effects on spine pain and addressed in all approaches to spine pain evaluation and management.

ARTICLE 3: PERIPHERAL NEUROPATHIC PAIN

Victor Wang, MD, PhD; Miroslav Bačkonja, MD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1363–1380.

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ABSTRACT

OBJECTIVE:

This article synthesizes current knowledge on neuropathic pain, with a brief review of mechanisms, diagnostic approaches, and treatment strategies to help neurologists provide effective and individualized care for patients with this complex condition.

LATEST DEVELOPMENTS:

The most promising developments in peripheral neuropathic pain are related to the molecular biology of the peripheral nervous system. Systematic molecular and genetic analyses of peripheral nerve terminals and dorsal root ganglia have advanced our understanding of the genetics of function and disease of peripheral nerves, as well as their physiology and clinical manifestations.

ESSENTIAL POINTS:

Peripheral neuropathic pain, similar to central neuropathic pain, is primarily influenced by the biology and pathophysiology of the underlying structures, peripheral sensory nerves, and their central pathways. The clinical course is widely variable in sensory symptoms and intensities, natural history, and response to treatments.

KEY POINTS

- When discussing painful peripheral neuropathies, patients usually describe typical painful sensations such as tingling, pins and needles, burning, and stabbing, termed *paresthesia* and *dysesthesia*, as most bothersome.
- In addition to paresthesia and dysesthesia, neuropathic pain frequently includes components of hyperalgesia (worsened pain from noxious stimuli) and allodynia (pain caused by innocuous stimuli).
- Most peripheral neuropathic pain disorders are chronic, with variability in symptom manifestations and disease course.
- There is no curative therapy for peripheral neuropathic pain and, in all cases, the therapy and management are primarily symptomatic, to relieve pain and improve function and quality of life.
- A wide range of disorders may present with peripheral neuropathic pain as a clinical feature.
- Several large clinical studies have demonstrated that painful neuropathies share distinct sensory pain phenotypes regardless of etiologic pathology, pointing to shared pain pathophysiologic mechanisms.
- To understand the dual peripheral and central nature of peripheral neuropathic pain pathophysiology, the diagnostic workup must account for peripheral nerve pathology and the sensory manifestations of peripheral and central sensitization.
- It is important to translate an understanding of the complexity of the pathophysiology of peripheral neuropathic pain into clinical evaluation, assessment, and treatment planning.
- Initial assessment of patients with neuropathic pain begins with taking a history of pain and its course, affected sensory and pain domains, and psychological and social aspects, including the impact of pain on function and quality of life.

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- Several patient-reported outcome tools have been developed to help clinicians assess the severity of neuropathic pain symptoms and response to treatment.
- Negative sensory phenomena almost always conform to the peripheral nerve anatomy, following the nerve, plexus, or root distribution, whereas positive sensory phenomena are frequently detectable outside of the peripheral nerve distribution because of the central sensitization phenomenon.
- There is no known curative therapy for peripheral neuropathic pain, and the main focus of neuropathic pain therapy is symptom control and improvement of function and quality of life.
- Neuropathic pain is best managed with a multimodal and multidisciplinary approach, which, in addition to pharmacotherapy, can include psychological support, training, and a comprehensive range of physical therapy modalities.
- Antiseizure medications are usually the first-line treatment for painful neuropathies.
- Duloxetine is the only US Food and Drug Administration (FDA)-approved antidepressant for use in painful diabetic neuropathy treatment, although several other antidepressants have been widely prescribed for painful neuropathy.
- Managing peripheral neuropathic pain requires a comprehensive and integrative approach that addresses the diverse aspects of the condition. This multidisciplinary and multimodal approach involves combining various therapeutic strategies to improve pain relief, enhance function, and promote overall well-being.
- Structured exercise programs tailored to individual needs can improve strength, flexibility, and coordination in patients with neuropathic pain. Low-impact exercises, such as swimming or tai chi, are often recommended to minimize stress on affected nerves.

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ARTICLE 4: CENTRAL NEUROPATHIC PAIN

Charles E. Argoff, MD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1381–1396.

ABSTRACT

OBJECTIVE:

This article provides an approach to the assessment, diagnosis, and treatment of central neuropathic pain.

LATEST DEVELOPMENTS:

Recent studies of the pathophysiology of central neuropathic pain, including evidence of changes in the expression of voltage-gated sodium channels and *N*-methyl-D-aspartate (NMDA) receptors, may provide the basis for new therapies. Other areas of current research include the role of cannabinoid-receptor activity and microglial cell activation in various animal models of central neuropathic pain. New observations regarding changes in primary afferent neuronal activity in central neuropathic pain and the preliminary observation that peripheral nerve blocks may relieve pain due to central neuropathic etiologies provide new insights into both the mechanism and treatment of central neuropathic pain.

ESSENTIAL POINTS:

In the patient populations treated by neurologists, central neuropathic pain develops most frequently following spinal cord injury, multiple sclerosis, or stroke. A multimodal, individualized approach to the management of central neuropathic pain is necessary to optimize pain relief and may require multiple treatment trials to achieve the best outcome.

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KEY POINTS

- The development of central neuropathic pain may occur following an injury of or in association with a disorder affecting the spinal cord or brain.
- Abnormal spinothalamic tract function is nearly always present in a person experiencing central neuropathic pain.
- Non-neuropathic pain may exist concurrently in a person experiencing central neuropathic pain.
- Mechanisms underlying central neuropathic pain include those involving both the peripheral and central nervous systems.
- Approximately 70% of spinal cord injuries are associated with a motor vehicle accident or a fall.
- Central neuropathic pain associated with spinal cord injury may occur concurrently with non-neuropathic pain associated with spinal cord injury, emphasizing the need for a formal neurologic assessment.
- Central poststroke pain is the most common type of central neuropathic pain.
- Stroke location is an important risk factor for the development of central poststroke pain.
- Chronic pain occurs in the majority of patients diagnosed with multiple sclerosis (MS).
- Central neuropathic pain is one of several types of pain that a person with MS may experience, and formal assessment for each type of MS-related pain should be completed.
- MS-related central neuropathic pain is more likely to occur in patients with a progressive MS course, older age, greater disability, and longer MS duration.
- Formal diagnostic criteria for central neuropathic pain associated with spinal cord injury, MS, or central poststroke pain have been recently proposed.
- There is a scarcity of large, high-quality randomized trials for central neuropathic pain.
- Multiple antiseizure medications have been evaluated for different central neuropathic pain states with mixed results.
- Based upon the results of two randomized controlled trials, duloxetine may be considered for MS-related neuropathic pain.
- Small studies suggest the potential role of IV lidocaine infusions for the treatment of central neuropathic pain.
- In addition to its role in the treatment of spasticity, onabotulinumtoxinA has been demonstrated to reduce pain in patients with spinal cord injury–related neuropathic pain when injected subcutaneously.
- Insufficient evidence is currently available regarding the effect of cannabinoids on central neuropathic pain.
- Insufficient evidence is available to broadly recommend chronic opioid therapy for the management of central neuropathic pain.
- Insufficient evidence is currently available to define the role of various neuromodulation approaches in the management of central neuropathic pain.
- Limited high-quality evidence exists for the treatment of central neuropathic pain, with the exception of pregabalin for spinal cord injury–related neuropathic pain. Commonly prescribed medications for central neuropathic pain do not have significant published evidence to support their use in general but may be considered on an individual basis.
- Nonpharmacologic treatments for central neuropathic pain may be considered in addition to or in place of pharmacologic therapies for people with central neuropathic pain.

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ARTICLE 5: OROFACIAL PAIN

Meredith Barad, MD; Marcela Romero-Reyes, DDS, PhD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1397–1426.

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ABSTRACT

OBJECTIVE:

This article explores the multiple etiologies, diagnosis, and management of orofacial pain.

LATEST DEVELOPMENTS:

Published in 2019, the International Classification of Orofacial Pain has become the internationally accepted classification system for primary and secondary facial pain. New discoveries in temporomandibular disorders have demonstrated that they are far more complex than the traditional dental mechanistic point of view. A 2020 consensus report released by the National Academies of Sciences, Engineering, and Medicine entitled "Temporomandibular Disorders: Priorities for Research and Care" highlighted this paradigm shift and its importance for patient care, education, and research.

ESSENTIAL POINTS:

Orofacial pain comprises many disorders with different etiologies and pathophysiologies. The subjectivity of the pain experience and the interrelated anatomy and physiology of the craniofacial area add to the complexity of diagnosis when the source and etiology of pain are not clear. As orofacial pain straddles the expertise of multiple disciplines, a multidisciplinary approach combining medication, physical therapy, and procedural and psychological strategies is essential in treating patients with orofacial pain.

KEY POINTS

- Given the complexity and difficulty in diagnosis, a multidisciplinary approach is the best strategy for diagnosing and treating orofacial pain.
- Odontogenic pain is the most common acute source of orofacial pain and is usually the result of pulp or periapical tissue pathology.
- Odontogenic pain can be referred to adjacent craniofacial structures as a form of secondary headache.
- Other painful oral problems include oral mucosal lesions, cancer-related pain, salivary gland pain, or mandibular or maxillary bone pain.
- Temporomandibular disorders are a constellation of musculoskeletal disorders involving the temporomandibular joint, the muscles of mastication, and their associated structures.
- Temporomandibular disorders are the most prevalent chronic orofacial pain.
- Temporomandibular disorders are comorbid with depression, poor sleep, primary headaches, and other chronic pain problems.
- Bruxism may influence temporomandibular disorder symptomatology in some individuals, but more research is necessary to establish evidence of causality.
- OnabotulinumtoxinA is not indicated as first-line management and is not US Food and Drug Administration (FDA) approved for the treatment of temporomandibular disorders, but it may be explored in refractory cases in consultation with an orofacial pain specialist.
- Trigeminal neuralgia is more common in women, appears to increase with age, and presents most frequently in the V2 distribution on the right side.
- One-half of patients with trigeminal neuralgia experience concomitant continuous pain.
- The examination in patients with classic trigeminal neuralgia is usually normal, and deficits in the distribution of the trigeminal nerve suggest trigeminal neuropathy.

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- Classical trigeminal neuralgia is thought to be caused by neurovascular compression.
- About 15% of patients with trigeminal neuralgia symptomology have secondary trigeminal neuralgia.
- The most common causes of secondary trigeminal neuralgia are multiple sclerosis and benign tumors.
- The goal of imaging in patients with trigeminal neuralgia is to look for evidence of vascular compression on the trigeminal nerve through nerve deviation, groove formation, or atrophy, and to exclude secondary causes.
- Treatment guidelines continue to suggest medical management as the first-line treatment of trigeminal neuralgia, with microvascular decompression being the most effective surgical option.
- Glossopharyngeal neuralgia causes similar pain to trigeminal neuralgia but is located in the ear, base of the tongue, roof of the mouth, and tonsillar fossa.
- Secondary glossopharyngeal neuralgia may be caused by Eagle syndrome, multiple sclerosis, tumors, trauma, and Chiari malformations.
- Treatment for classic glossopharyngeal neuralgia is similar to that for classic trigeminal neuralgia, with medication management being the first-line treatment and consideration of microvascular decompression after that.
- Nervus intermedius neuralgia is felt deep in the auditory canal and may also be due to vascular compression.
- The sphenopalatine ganglion is a parasympathetic ganglion contributing to sensation to the nasal cavity, sphenoid sinus, palate, and some of the nasopharynx and oropharynx.
- Interventional procedures, including implantable neuromodulation, to the sphenopalatine ganglion have been examined to treat cluster headache and other primary headache syndromes.
- Neuropathic pain is the pain state represented by damage to the nerve. While it can be idiopathic, it can be caused by herpes zoster or postherpetic neuralgia, multiple sclerosis, or mass lesions.
- Burning mouth syndrome is most commonly seen in women 3 to 12 years postmenopause.
- Burning mouth syndrome is considered secondary when it is caused by tongue thrust, poorly fitting dentures, fungal infections, allergies, medications, vitamin and mineral deficiencies, gastroesophageal reflux disease, diabetes, and hypothyroidism.
- Burning mouth syndrome is primary (idiopathic) when no secondary local or systemic source has been detected.
- Persistent idiopathic facial pain and persistent idiopathic dentoalveolar pain are challenging medical conditions for which neuromodulating medications are at present the best form of treatment.
- Primary headache syndromes can present in the face alone.

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ARTICLE 6: CHRONIC WIDESPREAD PAIN

Narayan R. Kissoon, MD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1427–1446.

ABSTRACT

OBJECTIVE:

This article reviews the potential etiologies of chronic widespread pain syndromes and outlines a practical approach to the management of patients with these disorders.

LATEST DEVELOPMENTS:

Recent updates to diagnostic criteria for primary chronic widespread pain syndromes have allowed for more effective diagnosis. Fibromyalgia is the most common presentation of chronic widespread pain, and the concept of nociplastic pain has been used to describe pain that is related to altered processing of pain sensory pathways. Research studies have provided a better

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understanding of the pathophysiology of the central augmentation that occurs in patients with nociplastic pain and fibromyalgia.

ESSENTIAL POINTS:

Primary chronic widespread pain and fibromyalgia have established diagnostic criteria in which chronic pain involves multiple defined regions and occurs for longer than 3 months. Evaluation of chronic widespread pain should be directed by the clinical presentation. Neurologic disease can present with chronic widespread pain but is accompanied by associated signs and symptoms. Patients with chronic widespread pain benefit from effective communication that validates concerns, provides an understandable explanation of the presenting symptoms, and sets realistic expectations in outcomes using a comprehensive multimodal care plan.

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KEY POINTS

- Chronic widespread pain and fibromyalgia have established diagnostic criteria in which chronic pain involves multiple defined regions and occurs for longer than 3 months.
- For chronic widespread pain to be diagnosed as fibromyalgia, it must be accompanied by associated symptoms such as fatigue, sleep disorders that may include waking unrefreshed, and cognitive symptoms.
- Fibromyalgia can present with pain that has neuropathic features and patients may have findings of allodynia on examination, but pain fluctuates and is outside dermatomal, myotomal, or sclerotomal distributions.
- Patients with fibromyalgia commonly present with comorbid disorders such as postural orthostatic tachycardia syndrome, persistent perceptual postural dizziness, mood disorders, migraine, and other chronic primary pain syndromes.
- Changes in gray matter volumes and small fiber intraepidermal nerve fiber density observed in patients with fibromyalgia are suspected to represent neuroplasticity rather than atrophy or neuropathy, respectively.
- Complex regional pain syndrome has validated diagnostic criteria that are useful in the diagnosis and include the presence of both symptoms and signs on examination.
- A patient-centered approach is used in the management of complex regional pain syndrome. When a patient is unable to participate in or has a failure to progress with rehabilitation, sympathetic blocks, spinal cord stimulation, or dorsal root ganglion stimulation may be of benefit.
- Parkinson disease can present with chronic widespread pain that is independent of musculoskeletal disease or dystonia and can have neuropathic features.
- Autoimmune IgG-mediated pain should be considered in patients presenting with a subacute onset (weeks to months) of multifocal neurologic signs and symptoms involving both the central and peripheral nervous systems.
- Hypermobile Ehlers-Danlos syndrome has distinct clinical findings of skin fragility and marfanoid features that allow it to be differentiated from joint hypermobility syndrome.
- All patients with chronic widespread pain should have a complete history and medical examination along with laboratory testing comprising a complete blood cell count and measurement of C-reactive protein, serum calcium, creatine phosphokinase, thyroid-stimulating hormone, and 25-hydroxyvitamin D levels.
- Opioids should be avoided in the treatment of patients with nociplastic chronic widespread pain and pathophysiologically may be detrimental given the observations of high endogenous opioids with low μ-opioid receptor binding observed in the setting of fibromyalgia.
- Patients with chronic widespread pain benefit from effective communication that validates concerns, provides an understandable explanation of the presenting symptoms, and sets realistic expectations in outcomes using a comprehensive multimodal care plan.

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ARTICLE 7: OPIOIDS AND CANNABINOIDS IN NEUROLOGY PRACTICE

Friedhelm Sandbrink, MD, FAAN; Nathaniel M. Schuster, MD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1447–1474.

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ABSTRACT

OBJECTIVE:

Opioid and cannabinoid therapies for chronic pain conditions including neuropathic pain are controversial. Understanding patient and prescribing factors contributing to risks and implementing risk mitigation strategies optimizes outcomes.

LATEST DEVELOPMENTS:

The ongoing transformation from a biomedical model of pain care toward a biopsychosocial model has been accompanied by a shift away from opioid therapy for pain, in particular for chronic pain. Opioid overdose deaths and opioid use disorder have greatly increased in the last several decades, initially because of increases in opioid prescribing and more recently associated with illicit drug use, in particular fentanyl derivatives. Opioid risk mitigation strategies may reduce risks related to opioid prescribing and tapering or discontinuation. Opioid therapy guidelines from the Centers for Disease Control and Prevention have become the consensus best practice for opioid therapy. Regulatory agencies and licensing medical boards have implemented restrictions and other mandates regarding opioid therapy. Meanwhile, interest in and use of cannabinoids for chronic pain has grown in the United States.

ESSENTIAL POINTS:

Opioid therapy is generally not recommended for the chronic treatment of neuropathic pain conditions. Opioids may be considered for temporary use in patients with severe pain related to selected neuropathic pain conditions (such as postherpetic neuralgia), and only as part of a multimodal treatment regimen. Opioid risk mitigation strategies include careful patient selection and evaluation, patient education and informed consent, querying the state prescription drug monitoring programs, urine drug testing, and issuance of naloxone as potential rescue medication. Close follow-up when initiating or adjusting opioid therapy and frequent reevaluation during long-term opioid therapy is required. There is evidence for the efficacy of cannabinoids for neuropathic pain, with meaningful response rates in select patient populations.

KEY POINTS

- Opioids for the treatment of chronic noncancer pain are generally not recommended for the chronic treatment of neuropathic pain or headache disorders.
- In 2022, the Department of Veterans Affairs/US Department of Defense recommended against initiating opioid therapy for chronic pain and suggested the use of buprenorphine instead of full μ-agonist opioids in patients on daily opioid therapy.
- The risks of tapering and discontinuing long-term opioid therapy include illicit opioid use, emergency department visits, opioid-related hospitalizations, mental health crises, and death from suicide or overdose.
- Despite the marked reduction in opioid prescribing for pain since 2012, deaths due to overdoses continue to escalate in the United States, with an annual rate of more than 100,000 overdose deaths since 2021.

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- While the deaths from prescribed opioids have decreased in recent years, illicit fentanyl overdoses are now the leading cause of opioid-related death.
- Many states require coprescription of naloxone for high-dosage opioid therapy or when in the context of benzodiazepines.
- Opioid overdose and opioid use disorder risk factors include the opioid therapy dosage and duration, concurrent use of sedatives, the use of extended-release or long-acting opioids, and the presence of substance use and mental health comorbidities.
- While overdose risk increases at 50 morphine milligram equivalent (MME) and higher, many patients with opioid overdose and exposure to prescription opioid medication are on dosages below this level.
- Dosage increases to greater than 50 MME/day are unlikely to substantially improve pain control for most patients, while overdose risk increases with dosage.
- Long-acting or slow-release opioids are associated with a higher risk for opioid overdose and should not be used for acute pain, when initiating opioid therapy, or for as-needed medication use.
- Methadone has been associated with a particularly high risk for respiratory depression and overdose, whereas buprenorphine has lower risk of respiratory depression and overdose death.
- The risk for opioid overdose is increased for individuals on long-term opioid therapy who also received concurrent long-term benzodiazepine therapy, with some risk, albeit lower, also noted for zolpidem.
- Screening tools including the Opioid Risk Tool for Opioid Use Disorder may be used to predict the risk of aberrant use behaviors or unhealthy opioid use for patients being considered for opioid therapy.
- Patients developing opioid use disorder while on prescribed opioid therapy should be provided urgent access to evidence-based treatments for opioid use disorder such as methadone or buprenorphine, and other pain treatments should be optimized.
- Methadone or buprenorphine therapy for opioid use disorder, if prescribed in patients with concurrent pain conditions, should be given in divided doses, usually 3 times a day, for better analgesic efficacy.
- Querying the state prescription drug monitoring program database is a standard safety practice when initiating and renewing opioid therapy.
- Urine drug testing should be considered before initiating opioid therapy, at least annually for patients on long-term opioid therapy, and more often according to risk.
- Prescribing of the opioid antagonist naloxone is considered an important risk mitigation strategy for patients on opioid therapy, especially in higher-risk situations.
- A common practice in opioid therapy monitoring is to document the "4 A's": analgesia, activities, adverse effects, and aberrant behavior.
- The use of the partial μ-opioid agonist buprenorphine for chronic pain is an emerging practice as it has a respiratory depression ceiling effect, unlike full μ-opioid agonists.
- While there has been great interest in cannabidiol (CBD) as a pain treatment, the evidence to date has not demonstrated pain benefits from CBD.
- CBD is a negative allosteric modulator of the CB1 receptor and reduces the psychoactivity of delta-9-tetrahydrocannabinol (THC). High CBD-to-THC ratio products are typically better tolerated, especially by cannabis-naive patients.
- There is evidence suggesting that THC has a narrow therapeutic window for neuropathic pain, with therapeutic benefit at subintoxicating dosages or at dosages with limited psychoactive effects.
- Cannabis use disorder is present in nearly 10% of users and about one-third of daily users.
- Compulsive hot water bathing or showering for symptomatic relief is pathognomonic for cannabis hyperemesis syndrome.
- Cannabis has biphasic effects on nausea. With persistent high-dose use, it can be proemetic.

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ARTICLE 8: NEUROMODULATION FOR NEUROPATHIC PAIN SYNDROMES

Prasad Shirvalkar, MD, PhD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1475–1500.

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ABSTRACT

OBJECTIVE:

This article reviews the principles, applications, and emerging trends of neuromodulation as a therapeutic approach for managing painful neuropathic diseases. By parsing evidence for possible mechanisms of action and clinical trial outcomes for various diseases, this article focuses on five common therapy modalities: cutaneous, peripheral nerve, spinal cord, and brain stimulation, and intrathecal drug delivery.

LATEST DEVELOPMENTS:

Recent advances in both invasive and noninvasive neuromodulation for pain have introduced personalized and closed-loop techniques, integrating real-time feedback mechanisms and combining therapies to improve physical and psychosocial function. Novel stimulation waveforms may influence distinct neural tissues to rectify pathologic pain signaling.

ESSENTIAL POINTS:

With appropriate patient selection, peripheral nerve stimulation or epidural stimulation of the spinal cord can provide enduring relief for a variety of chronic pain syndromes. Newer technology using high frequencies, unique waveforms, or closed-loop stimulation may have selective advantages, but our current understanding of therapy mechanisms is very poor. For certain diagnoses and patients who meet clinical criteria, neuromodulation can provide profound, long-lasting relief that significantly improves quality of life. While many therapies are supported by data from large clinical trials, there is a risk of bias as most clinical studies were funded by device manufacturers or insurance companies, which increases the importance of real-world data analysis. Emerging methods like invasive or noninvasive brain stimulation may help us dissect basic mechanisms of pain processing and hold promise for personalized therapies for refractory pain syndromes. Finally, intrathecal delivery of drugs directly to segments of the spinal cord can also modify pain signaling to provide therapy for severe pain syndromes.

KEY POINTS

- **The four key adjustable parameters that control electrical stimulation are contact polarity, pulse width, frequency, and amplitude.**
- **Low-frequency stimulation typically replaces painful sensations with a tingling or vibratory paresthesia in the nerve distribution, while high-frequency stimulation can provide paresthesia-free pain relief.**
- **Gate control theory describes spinal cord mechanisms by which large-diameter and small-diameter fibers interact to "gate out" ascending pain signals.**
- **The SAFE principles offer clinical guidance for treatment algorithms involving implanted neuromodulation therapies: s**afety, **a**ppropriateness, **f**iscal neutrality, and **e**fficacy.
- **Peripheral nerve stimulation involves stimulating nerve axons by placing a fine electrode wire within 1 cm and is most appropriate for focal pain syndromes and neuralgias.**
- **Spinal cord stimulation is the most common type of electrical neuromodulation for chronic pain, with over 30,000 patients undergoing trial or permanent implant yearly worldwide.**

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- Despite the various approved indications for spinal cord stimulation therapy, group-level clinical outcome data remain controversial due to few studies with rigorous blinding or placebo control.
- Complex regional pain syndrome is a rare pain syndrome typically affecting one limb that involves neuroimmune, vasomotor, sudomotor, and trophic changes. Dorsal root ganglion stimulation is the only approved therapy for lower-extremity complex regional pain syndrome.
- In the case of a potential infection near spinal cord stimulator hardware, it is urgent to completely explant all hardware.
- While drug spread can be influenced by infusion rate or concentration, intrathecal drug delivery is typically best suited for focal pain syndromes involving one to two spinal levels.
- Although intrathecally delivered medications are minimally present in systemic circulation, abruptly discontinuing the infusion due to pump malfunction or a missed refill appointment could precipitate withdrawal. This can be life-threatening if using intrathecal baclofen.
- Deep brain stimulation for chronic pain has been studied since 1960 but remains off label due to the lack of a single "best target" for all patients and the development of tolerance to stimulation over time.
- Motor cortex stimulation involves stimulating the superficial motor cortex with implanted electrode arrays. Potential response for pain control may be identified by first using transcranial magnetic stimulation noninvasively.
- Transcranial magnetic stimulation for pain uses noninvasive magnetic fields through the scalp to induce electrical field stimulation on the primary motor cortex over repeated daily sessions.
- Although therapeutic effects of transcranial magnetic stimulation for pain are short lived, usually dissipating by 1 month, transcranial magnetic stimulation can be used to identify candidates who would benefit from the permanent implant of a motor cortex stimulator.

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ARTICLE 9: CHRONIC PAIN PSYCHOLOGY IN NEUROLOGY PRACTICE

Mirsad Serdarevic, PhD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1501–1516.

ABSTRACT

OBJECTIVE:

This article reviews the latest literature regarding chronic pain epidemiology and describes pain-specific psychological factors associated with the development and maintenance of chronic pain, mental health conditions that co-occur with chronic pain, and advances in the psychobehavioral treatment of chronic pain, including established treatments (ie, cognitive behavioral therapy [CBT], acceptance and commitment therapy, and mindfulness-based stress reduction) and emerging treatments (ie, pain reprocessing therapy).

LATEST DEVELOPMENTS:

In addition to CBT and acceptance and commitment therapy for pain, numerous other psychological treatment modalities have been integrated into chronic pain management, including mindfulness-based stress reduction, mindfulness meditation, chronic pain self-management, relaxation response, pain neuroscience education, biofeedback, hypnosis, and, more recently, integrative psychological treatment for centralized pain. This article gives an overview of these methods and contextualizes their use within the standard psychological treatment of chronic pain.

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ESSENTIAL POINTS:

Guided by the biopsychosocial treatment model, pain psychologists use numerous evidence-based psychological methods to treat patients with chronic pain conditions. Familiarity with the psychological tools available for pain management will aid neurologists and their patients in navigating the psychological aspects of living with chronic pain.

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KEY POINTS

- The incidence of chronic pain is 52.4 cases per 1000 people per year.
- Given that chronic pain is a complex biopsychosocial disease that can affect all aspects of life including mood, social life, cognition, physical health, and functioning, it comes as no surprise that interdisciplinary treatment is the only reliable treatment for chronic pain as medication alone and procedures alone cannot break the pain cycle.
- Acceptance and commitment therapy and cognitive behavioral therapy are the psychological pain interventions that have shown the strongest evidence of benefit and cost effectiveness.
- Research on the effectiveness of cognitive behavioral therapy for pain in patients with chronic pain has shown gray matter volume increases in the posterior parietal cortex, bilateral dorsolateral prefrontal cortex, and other sensory, motor, and affective regions of the brain also associated with pain control.
- Cognitive behavioral therapy for pain is about changing one's relationship with and response to pain to lessen its impact on functioning and quality of life and focuses on how one's beliefs, emotions, physiologic responses, and behaviors affect the experience of pain.
- The gate control theory of pain suggests that pain signals do not automatically or directly reach the brain; rather, a "gate mechanism" that controls the amount of pain signals that reach the brain is located within the spinal cord, and more pain signals pass through when the gate is open than when it is closed.
- Acceptance and commitment therapy is a psychological intervention that integrates many cognitive behavioral therapy–related variables into core therapeutic processes. The goal of acceptance and commitment therapy is to increase psychological flexibility and reduce pain's dominance in a person's life.
- Mindfulness-based treatments of chronic pain, including most widely used mindfulness-based stress reduction techniques, aim to cultivate acceptance through nonjudgmental, purposeful attention to the present moment.
- Mindfulness-based treatments for chronic pain can be used alone or in combination with other treatments, such as cognitive behavioral therapy and acceptance and commitment therapy.
- Biofeedback provides immediate audible or visual cues to the patient regarding changes in physiologic activity (eg, heart rate, muscle tension, respiration) using precise instrumentation. Patients gain awareness and control of their physiologic responses through such feedback, leading to improved psychological and physiologic functioning.
- Clinical hypnosis for chronic pain treatment involves the patient entering a state of focused attention, allowing for more openness to suggestions for changes in behaviors, sensations, and thoughts. Clinical hypnosis is divided into two phases: an induction phase, followed by specific suggestions for therapeutic change.
- Integrative psychological treatment for centralized pain, which includes pain reprocessing therapy, focuses on treating patients whose pain is either partially or completely centralized (ie, nociplastic or somatoform).
- In pain reprocessing therapy, patients learn to view their pain through a "safety lens" and remind themselves that there is no danger, and while the sensations are real, they are also temporary.
- The ADDRESSING approach (age and generational influences, developmental and acquired disabilities, religion and spiritual orientation, ethnicity, socioeconomic status, sexual orientation, indigenous heritage, national origin, gender) provides a framework for understanding the impact of a clinician's worldview of different cultures on patient care.

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ARTICLE 10: PEDIATRIC PAIN

Alyssa Lebel, MD; Nathaniel M. Schuster, MD. Continuum (Minneap Minn). October 2024; 30 (5 Pain Management in Neurology):1517–1535.

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ABSTRACT

OBJECTIVE:

This article reviews pain disorders encountered in pediatric neurology practice and provides current information regarding the assessment and treatment of pediatric chronic pain.

LATEST DEVELOPMENTS:

Data about pediatric pain management remain sparse, owing to a dearth of controlled trials and longitudinal studies in these patients. However, the field of pain management and understanding of central and peripheral pain processing has expanded to allow more effective treatment of a broad group of children and adolescents with pain associated with neurologic disease. Neuroimaging visualizes sensory and nonsensory systems, and genetic markers of sensitivity and disease may guide specific therapy. The concept of central sensitization in chronic pain disorders has supported the development of multidisciplinary paradigms for the comprehensive care of these patients.

ESSENTIAL POINTS:

Pain involves sensory activation and central nervous system modulation in pediatric patients. Pediatric neurologists should be prepared to define, investigate, and treat pain disorders in this complex patient population. Appropriate interventions during childhood may attenuate or prevent chronic pain later in life. Current interventions include behavioral, physical, and pharmacologic approaches, as well as potential noninvasive tools for neuromodulation. Research is progressing in sensory measurement, neuroimaging, genetics, and neuroinflammation to guide future targeted therapies.

KEY POINTS

- The prevalence of chronic pain in children is widespread and is more common in females. Pediatric chronic pain prevalence in low-income and middle-income countries is underreported in the literature, and yet is a leading cause of morbidity.
- Pain is a frequent component of rare neurometabolic diseases.
- Chronic pain assessment can be individualized through self-report measures depending on the patient's needs and developmental and cognitive levels.
- The neurologic examination for patients with pain includes assessment of small sensory fiber function.
- Neuroimaging studies illustrate that pain disorders are, at their root, disorders of the brain.
- Maladaptive changes within the nociceptive network coincide with maturation of the nervous system, and thus pediatric neuropathic pain disorders may differ from adult conditions regarding presentation, prognosis, and treatment.
- Studies support psychological treatment for chronic pain, with cognitive behavioral therapy recommended as a best practice.
- Studies have shown that targeting the patient's relationship with their pain in therapy is a powerful intervention.
- The evaluation of patients unable to assess or verbalize their pain due to intellectual delay relies heavily on provider assessment.
- Pain assessment in patients with cerebral palsy is often complicated by dysregulated sleep patterns, myoclonus, and seizures.

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